

USSN: 09/719,410
Amdt. Dated 10/20/04
Reply to Office Action of 10/14/04
Page 2 of 10

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1-9. (cancelled)

10. (currently amended) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with non-insulin dependent diabetes mellitus (NIDDM), comprising:

administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 ~~and a pharmaceutical carrier, thereby treating impaired glucose tolerance, said composition containing an amount of said compound effective to enhance the regularity of insulin responses, and the amplitude thereof, in reaction to changes in plasma glucose.~~

11. (original) The method of claim 10 wherein the receptor binding compound is selected from (a) a peptide which comprises the amino acid sequence of glucagon-like peptide-1, and (b) a variant peptide comprising an amino acid sequence that differs from the sequence of glucagon-like peptide-1 by one or more substitutions, deletions or insertions.

12. (original) The method of claim 11 wherein the receptor binding compound is glucagon-like peptide-1.

13. (currently amended) The method of claim 11 wherein the receptor binding compound is glucagon-like peptide-1 (7-37) which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly SEQ ID NO:3 (~~SEQ ID NO:3~~).

USSN: 09/719,410
Amdt. Dated 10/20/04
Reply to Office Action of 10/14/04
Page 3 of 10

14. (currently amended) The method of claim 11 wherein the receptor binding compound is glucagon-like peptide-1 (7-36) amide which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg (NH₂) SEQ ID NO:4 (~~SEQ ID NO:4~~).
15. (original) The method of claim 11 wherein the receptor binding compound is a variant peptide in which the combination of the substitutions, deletions and insertions in the amino acid sequence does not differ by more than ten amino acids from the amino acid sequence of glucagon-like peptide-1.
16. (original) The method of claim 10 wherein the receptor binding compound is expressed by a polynucleotide.
17. (currently amended) The method of claim 10 wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000 daltons.
18. (currently amended) The method of claim 10 wherein the step of administering is selected from the group consisting of intravenous, subcutaneous, intramuscular, intraperitoneal ~~interperitoneal~~, injected depot with sustained release, deep lung insufflation with sustained release, buccal or patch.
19. (original) The method of claim 10, further comprising administering an agent that enhances the half-life in vivo of said receptor binding compound.
20. (original) The method of claim 19 wherein the agent is administered concurrently with the composition.

USSN: 09/719,410
Amdt. Dated 10/20/04
Reply to Office Action of 10/14/04
Page 4 of 10

21. (original) The method of claim 19 wherein the agent is covalently linked to the receptor binding compound.
22. (original) The method of claim 18 wherein intravenous administration is in a dose range of from about 0.3 to about 2.0 pmol/kg per minute.
23. (original) The method of claim 18 wherein continuous subcutaneous administration is in a dose range of from about 1.0 to about 20.0 pmol/kg per minute.
24. (currently amended) The method of claim 1, wherein said composition contains
~~A method for treating a human with impaired glucose tolerance, comprising:~~
~~administering to the human a composition comprising a compound which binds to~~
~~a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, said composition~~
containing an amount of said compound effective to retard or arrest the loss of plasma glucose control or [[and]] the development of non-insulin dependent diabetes mellitus.
25. (original) The method of claim 24 wherein the receptor binding compound is selected from (a) a peptide which comprises the amino acid sequence of glucagon-like peptide-1, and (b) a variant peptide comprising an amino acid sequence that differs from the sequence of glucagon-like peptide-1 by one or more substitutions, deletions or insertions.
26. (original) The method of claim 25 wherein the receptor binding compound is glucagon-like peptide-1.
27. (currently amended) The method of claim 25 wherein the receptor binding compound is glucagon-like peptide-1 (7-37) which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly SEQ ID NO:3 (~~SEQ ID NO:3~~).

USSN: 09/719,410
Amdt. Dated 10/20/04
Reply to Office Action of 10/14/04
Page 5 of 10

28. (currently amended) The method of claim 25 wherein the receptor binding compound is glucagon-like peptide-1 (7-36) amide which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg (NH₂) SEQ ID NO:4 (~~SEQ ID NO:4~~).

29. (original) The method of claim 25 wherein the receptor binding compound is a variant peptide in which the combination of the substitutions, deletions and insertions in the amino acid sequence does not differ by more than five amino acids from the amino acid sequence of glucagon-like peptide-1.

30. (original) The method of claim 24 wherein the receptor binding compound is expressed by a polynucleotide.

31. (currently amended) The method of claim 24 wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000 daltons.

32. (currently amended) The method of claim 24 wherein the step of administering is selected from the group consisting of intravenous, subcutaneous, intramuscular, intraperitoneal ~~interperitoneal~~, injected depot with sustained release, deep lung insufflation with sustained release, buccal or patch.

33. (original) The method of claim 32 wherein intravenous administration is in a dose range of from about 0.1 to about 10.0 pmol/kg per minute.

34. (original) The method of claim 32 wherein continuous subcutaneous administration is in a dose range of from about 0.1 to about 75.0 pmol/kg per minute.

USSN: 09/719,410
Amdt. Dated 10/20/04
Reply to Office Action of 10/14/04
Page 6 of 10

35. (currently amended) The method of claim 10, wherein A method for treating an individual with impaired glucose tolerance comprising:

~~administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, wherein said composition contains an amount of said compound effective to improve entrainment of $[(\beta)]$ -cell insulin secretory responses to exogenous glucose oscillations.~~

36. (currently amended) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with NIDDM comprising:

administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 ~~and a pharmaceutical carrier~~, said composition containing an amount of said compound effective to enhance a normalization of insulin secretory patterns in impaired glucose tolerance, thereby treating impaired glucose tolerance.

37. (currently amended) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with NIDDM comprising:

administering to said individual a compound which binds to a receptor for glucagon-like peptide-1 ~~and a pharmaceutical carrier~~, said composition containing an amount of said compound effective to reduce plasma insulin levels in an individual with impaired glucose tolerance, thereby treating impaired glucose tolerance.

38. (currently amended) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with NIDDM comprising:

administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 ~~and a pharmaceutical carrier~~, said composition containing an amount of said compound effective to reduce insulin

USSN: 09/719,410
Amdt. Dated 10/20/04
Reply to Office Action of 10/14/04
Page 7 of 10

resistance in an individual with impaired glucose tolerance, thereby treating impaired glucose tolerance.

39. (currently amended) A method for reducing a treating an individual whose symptoms indicate increased risk of a cardiovascular event comprising:

administering to an said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, thereby reducing the risk of a cardiovascular event, said composition containing an amount of said compound effective to enhance the regularity of insulin responses, and the amplitude thereof, in reaction to changes in plasma glucose, and to reduce plasma insulin levels.

40. (currently amended) A method for reducing a treating an individual whose symptoms indicate increased risk of a cerebrovascular event comprising:

administering to an said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, thereby reducing the risk of a cerebrovascular event, said composition containing an amount of said compound effective to enhance the regularity of insulin responses, and the amplitude thereof, in reaction to changes in plasma glucose, and to reduce plasma insulin levels.

41 (new) The method according to claim 10, wherein said composition contains an amount of said compound effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose.

42. (new) The method of claim 39, wherein said composition contains an amount of said compound effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose, thereby reducing the risk of a cardiovascular event.

43. (new) The method of claim 40, wherein said composition contains an amount of said compound effective to enhance the regularity of insulin responses, or the amplitude

USSN: 09/719,410
Amdt. Dated 10/20/04
Reply to Office Action of 10/14/04
Page 8 of 10

thereof, in reaction to changes in plasma glucose, thereby reducing the risk of a cerebrovascular event.

44. (new) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with non-insulin dependent diabetes mellitus (NIDDM), comprising:
- administering to said individual a composition comprising an exendin or a variant of said exendin comprising an amino acid sequence that differs from the sequence of exendin by one or more substitutions, deletions or insertions, thereby treating impaired glucose tolerance.
45. (new) The method of claim 44 wherein the exendin is exendin 3, SEQ ID NO:7.
46. (new) The method of claim 44, wherein the exendin is exendin 4, SEQ ID NO:9.
47. (new) The method of claim 44, wherein the combination of substitutions, deletions or insertions of the variant does not differ by more than ten amino acids from the amino acid sequence of the exendin.
48. (new) The method of claim 44, wherein the step of administration is selected from the group consisting of intravenous, subcutaneous, intramuscular, intraperitoneal, injected depot with sustained release, deep lung insufflation with sustained release, buccal or patch.
49. (new) The method of claim 44, wherein the exendin or variant thereof is administered in a range of 0.005 nmol/kg to 20 nmol/kg.
50. (new) The method of claim 44, wherein said composition contains an amount of the exendin or variant thereof effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose.

USSN: 09/719,410
Amdt. Dated 10/20/04
Reply to Office Action of 10/14/04
Page 9 of 10

51. (new) The method of claim 44, wherein said composition contains an amount of the exendin or variant thereof effective to retard or arrest the loss of plasma glucose control or the development of non-insulin dependent diabetes mellitus:

52. (new) The method of claim 44, wherein said composition contains an amount of the exendin or variant thereof effective to enhance a normalization of insulin secretory patterns in impaired glucose tolerance.

53. (new) The method of claim 44, wherein said composition contains an amount of the exendin or variant thereof effective to reduce plasma insulin levels in an individual with impaired glucose tolerance.

54. (new) The method of claim 44, wherein said composition contains an amount of the exendin or variant thereof effective to reduce insulin resistance in an individual with impaired glucose tolerance.

55. (new) A method for reducing a risk of a cardiovascular event comprising:
administering to an individual a composition comprising an exendin or a variant thereof, thereby reducing the risk of a cardiovascular event.

56. (new) The method of claim 55, wherein said composition contains an amount of the exendin or variant thereof effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose.

57. (new) A method for reducing a risk of a cerebrovascular event comprising:
administering to an individual a composition comprising an exendin or a variant thereof, thereby reducing the risk of a cerebrovascular event.

58. (new) The method of claim 57, wherein said composition contains an amount of the exendin or variant thereof effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose.